

Lung function in type 1 Saudi diabetic patients

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ABSTRACT

Objectives: To determine the effects of type 1 diabetes mellitus on lung function and its gravity in relation to the duration of disease.

Methods: We carried out this study in the Department of Physiology, College of Medicine and Diabetic Center, King Abdul-Aziz University Hospital, King Saud University, Riyadh, Saudi Arabia during the period 2003-2004. We randomly selected a group of 27 apparently healthy volunteer Saudi male type 1 diabetic patients with age ranging from 19-70 years. We matched the diabetic patients with another group of 27 control healthy male subjects in terms of age, height, weight and socioeconomic status. Both groups met with exclusion criteria as per standard. We performed spirometry on an Electronic Spirometer (Schiller AT-2 Plus, Switzerland)

and compared the results by a student t-test (2-tailed).

Results: Type 1 diabetic patients showed a significant reduction in the forced vital capacity and forced expiratory volume in one second (FEV₁) relative to their matched controls. However, there was no significant difference in the forced expiratory ratio, forced expiratory flow; forced expiratory flow and peak expiratory flow (PEF) between the groups.

Conclusion: It is concluded that lung function in type 1 diabetic patients is impaired by a decrease in FVC and FEV₁ as compared to their matched controls. Additionally, the years of disease showed a dose-response effect on lung function.

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Type 1 (insulin-dependent) diabetes mellitus is a serious, progressive multifactorial disease associated with several chronic complications that are mainly a consequence of macro vascular and micro vascular damage,¹ and predispose to excess morbidity and premature mortality. Type 1 diabetes mellitus accounts for over 10% of the total diabetic cases,² and incidence is increasing globally both in low and high frequency populations.³ Diabetes mellitus, although worldwide in distribution, are more commonly seen in the developed European countries, US and Middle-Eastern countries.⁴ The prevalence rate is higher in Saudi Arabia compared with other Arab countries, for example, United Arab Emirates, Kuwait, Yemen, Qatar, Oman, Bahrain,

Jordan and Libya. Recent studies suggest that more than 100,000 people in the Arabian Peninsula suffer from type 1 diabetes with approximately 6000 new cases added each year.⁵ The most probable reason for this high incidence in Saudi Arabia is the rapid economical development over the last 20 years, resulting in the adaptation of western life style with respect to nutritional habits and physical activity, which results in a high incidence of diabetes mellitus.⁶ Diabetes mellitus associates with long term damage, dysfunction and failure of various organs,⁷ and its complications are mostly due to macrovascular and microvascular damage, including cardiovascular disease, nephropathy, diabetic retinopathy, neuropathy and lung damage.⁸ The

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histopathologic evidence of the involvement of lungs in subjects with diabetes mellitus showed thickened alveolar walls, alveolar capillary walls and the pulmonary arteriolar walls, these histological changes in the lungs are becoming a cause of pulmonary dysfunction.^{9,10} It is also demonstrated that both the pulmonary and renal complications of diabetes share a similar microangiopathic background.¹¹ These complications have a significant impact on the quality of life of affected individuals,^{12,13} and impose a heavy burden on health care provider's world wide.¹ In spite of availability of effective interventions, long term disabling complications often accompany diabetes, which are primary causes of clinical, social and economic burdens of the disease.¹⁴ However, great attention was centered on the complications of diabetes, including cardiovascular disease, nephropathy, diabetic retinopathy, neuropathy, but, the pulmonary complications of diabetes mellitus poorly characterized. While, some authors reported normal pulmonary function,¹⁵ others found abnormalities in lung volumes, pulmonary mechanics, and diffusing capacity.^{16,17} In addition, many studies do not consider the association with a dose-response effect between years of disease and pulmonary function and with no explanation by promising factors such as age, height, weight, smoking or socio-economic status. Moreover, the point which deserves discussion is that the physicians should know the size of problem of pulmonary complications; as a consequence, the novel techniques used in the treatment of diabetes mellitus, such as insulin pump inhaler. Therefore, we designed the present study to determine the effects of type 1 diabetes mellitus on lung function.

Methods. This study was conducted in the Department of Physiology, College of Medicine and Diabetic Center, King Abdul-Aziz University Hospital (KAUH), King Saud University, Riyadh, Saudi Arabia during the period 2003-2004. One hundred medical files of type 1 diabetic patients were reviewed, patients were called at the Diabetic Centre KAUH and clinically interviewed. A detailed history was taken to determine whether they would be included in the study or not on the foundation of the exclusion criteria. They were questioned with regard to smoking cigarettes or other tobacco products. After the initial interviews, 27 apparently healthy male type 1 diabetic patients with a mean age of 40.25 ± 3.02 years (mean \pm SEM), range 19-71 years with mean duration of disease 11.62 ± 1.40 years (mean \pm SEM), range 2-30 years, were selected and 73 were excluded. Controls were selected in a similar manner to that of the diabetics, from approximately 100 interviewed, 27 apparently healthy male control subjects were selected with a mean age of 39.37 ± 3.37 years (mean \pm SEM), range 19-71 years.

Diabetic patients were individually matched for age, height, and weight with controls. It was attempted that the matching between both groups was ± 3 years for age, ± 4 cm for height, ± 5 kg for weight, out of all these pairs none had more than one difference in anthropometry, if any one pair did not fall within the age matching, it was within the height and weight matching. Overall, there were no significant differences in the anthropometric means, in the combined or stratified data. Age and height were given more emphasis for matching as these 2 relate better to lung function than weight.¹⁸ Controls were of a similar community with socio-economic group relative to diabetics; both were assessed by a detailed history. All subjects were non-smokers, who had never smoked. All subjects completed a questionnaire, which included introduction, consent form and the anthropometric data was obtained by one of the member of investigating team. The Ethics Committee, College of Medicine, King Khalid University Hospital, King Saud University approved the study.

Subjects with gross abnormalities of the vertebral column, thoracic cage, restricted joint mobility, known history of acute or chronic respiratory infections, neuromuscular disease, malignancy, cardiopulmonary disease and those who had undergone major abdominal or chest surgery were excluded from participating in the study. In addition, subjects with current or previous drug or tobacco history (smoked or chewed) and addicts were excluded. Also, patients with known complications of diabetes mellitus such as diabetic neuropathy, nephropathy, and retinopathy were also excluded from the study.

Spirometry was performed on an electronic spirometer (Schiller AT-2 Plus Switzerland). All pulmonary function tests were carried out at a fixed time of the day (10.00–14.00 hours) to minimize diurnal variation.¹⁹ The apparatus was calibrated daily and operated within the ambient temperature range of 20-25°C. The precise technique in executing various lung function tests for the present study was based on the operation manual of the instrument with special reference to the official statement of the American Thoracic Society of Standardization of Spirometry (1987).²⁰ After taking a detailed history and anthropometric data, the subjects were informed about the whole maneuver. The subjects were encouraged to practice this maneuver before doing the pulmonary test. The test was performed with the subject in the standing position by using a nose clip. The test was repeated 3 times after adequate rest, and results were printed with built in printer available in the spirometer. These parameters were forced vital capacity (FVC), force expiratory volume in one second (FEV₁), forced expiratory ratio (FEV₁/FVC), forced expiratory flow (FEF_{25-75%}) and peak expiratory flow (PEF).

Statistical analysis was conducted using the Statistical Analysis for Social Sciences (version 10 for windows) and students t-test was applied for independent group (2-tailed), initially on all matched pairs of subjects, and then in 3 groups divided by their mean duration of disease. The level of significance was taken as $p < 0.05$.

Results. The results are presented as an overall group and stratified according to mean duration of disease in the type 1 diabetic patients (6.92 ± 1.08 years and 18.57 ± 1.02 years). In **Tables 1-4**, the formal statistical comparison of the 'matching' variables (age, height and weight) was thought to be appropriate, as these variables are inherently similar for the 2 groups; hence, statistical confirmation of this fact is not discussed.

Overall group results. Lung function data for type 1 diabetic patients and their matched controls are shown in **Table 1**. Type 1 diabetic patients had statistically significant reductions in FVC and FEV₁. However, the means for FEV₁/FVC%, FEF_{25-75%}, FEF_{75-85%} and PEF were not significantly different. The mean duration of disease for the type 1 diabetics was 11.62 ± 1.40 years (mean \pm SEM), range 2-30 years.

Lung function parameters for type 1 diabetic patients with mean duration of disease 6.92 ± 1.8 (range 2-13) years compared with their matched control. **Table 2** summarizes the comparison of the lung function parameters between type 1 diabetic patients and their matched control group. There was no significant difference between the means of any lung function data between the groups. The mean duration of disease for type 1 diabetic patients was 6.92 ± 1.08 years (mean \pm SEM), range 2-13 years.

Lung function parameters for type 1 diabetic patients with mean duration of disease 18.57 ± 1.02 (range 15-30) years compared with their matched control. Lung function data for type 1 diabetic patients and their matched controls are shown in **Table 3**. Type 1 diabetic patients had statistically significant reductions in FVC and FEV₁. However, the means for FEV₁/FVC%, FEF_{25-75%}, FEF_{75-85%} and PEF were not significantly different. The mean duration of disease in type 1 diabetics was 18.57 ± 1.02 (mean \pm SEM), range 15-30 years.

Lung function data comparison among the 2 groups of type 1 diabetic patients. **Table 4** demonstrates the lung function parameters among Type 1 diabetic patients with mean duration of disease 7.63 ± 1.14 (range 2-13) years, compared with another group of matched type 1 diabetic patients with mean duration of disease 17.1 ± 0.62 (range 15-20) years. Type 1 diabetic patient with greater mean duration of disease 17.1 ± 0.62 years showed a significant reduction in FEV₁, FEV₁/FVC%, FEF_{25-75%} and PEF relative to their

other matched group of type 1 diabetic patients with less mean duration of disease 7.63 ± 1.14 (range 2-13) years. Similarly, the percentage change was also decreased with the greater mean duration of disease.

Discussion. The present study shows impaired lung function parameters (FVC and FEV₁) and this decline is associated with the mean duration of a disease on pulmonary function impairment in type 1 diabetic patients compared to their matched controls. We explained this association by age, height, weight and smoking. Asanuma et al,²¹ Lange et al,¹⁷ and Boulbou et al,⁸ reported reduction in FVC and FEV₁ in diabetic patients compared to control subjects. Similarly, Cazzato et al,²² conducted a cross-sectional study to assess the pulmonary function in children with type 1 diabetes mellitus and reported that the FVC, FEV₁ significantly lower in diabetics than controls. Our results confirm these results. In contrary Benbassat et al,²³ showed that the FVC, FEV₁ and FEF_{25-75%} were within the predicted values. The most probable reason for the contradiction, is that Benbassat et al, studied pulmonary function among a group of diabetic patients by considering their predicted values, but they did not compare their results with the matched control group. Innocenti et al,²⁴ described the abnormalities of pulmonary function tests in type 1 diabetic patients and demonstrated that diabetic patients had a reduced FVC, FEV₁ compared to their matched controls. Our results correlate these results. In addition, our results are in agreement with that of Primhak et al,¹⁶ Makkar et al,²⁵ and Boulbou et al,⁸ as they performed spirometry in patients with type 1 diabetes mellitus compared with their controls and reported that the type 1 diabetic patients had a reduced FVC, FEV₁, PEF and MEF 25-75% compared to their matched control. Rosenecker et al,²⁶ reported a significant decrease in FVC and FEV₁ in patients with diabetes mellitus over the 5-year study period, whereas patients without diabetes did not show a significant decline during the study period. In addition, Bell et al,²⁷ measured the lung volumes in 28 young adult men with type 1 diabetes mellitus of long duration compared with 16 age and height-matched adult men without diabetes. Their results showed reduced values for vital capacity, forced expiratory volume in one second for the type 1 diabetic patients compared to the control subjects. The results were consistent with reduced lung volumes in type 1 diabetic patients and related to duration of diabetes. Our results based on the duration of the disease are in agreement with the results observed by Bell et al. On the contrary, Maccioni and Colebatch²⁸ studied the effect of diabetes mellitus on pulmonary function in 22 type 1 diabetic patients and showed

Table 1 - Anthropometric and lung function data for type 1 diabetic patients compared with their matched controls.

Parameter	Diabetic patients (mean \pm SEM) (n=27)	Control subjects (mean \pm SEM) (n=27)	Percentage change (%)	p-value
Age (years)	40.25 \pm 3.02	39.37 \pm 3.37	-2.23	NS
Height (cm)	170.72 \pm 1.34	171.88 \pm 1.38	+0.67	NS
Weight (kg)	75.58 \pm 2.09	78.62 \pm 2.20	+3.86	NS
FVC (litres)	3.68 \pm 0.12	4.25 \pm 0.12	+13.14	p=0.001
FEV ₁ (litres)	3.10 \pm 0.13	3.51 \pm 0.10	+11.68	p=0.02
FEV ₁ /FVC%	84.05 \pm 2.10	82.70 \pm 0.90	-1.63	NS
FEF _{25-75%} (litres/s)	3.62 \pm 0.25	3.99 \pm 0.20	+9.27	NS
FEF _{75-85%} (litres/s)	1.41 \pm 0.13	1.23 \pm 0.10	-14.63	NS
PEF (litres/sec)	6.55 \pm 0.53	6.79 \pm 0.38	+3.53	NS
FVC - forced vital capacity, FEV ₁ - forced expiratory volume in one second, FEF - forced expiratory flow, PEF - peak expiratory flow, FEV ₁ /FVC% - forced expiratory ratio, NS - not significant, s - seconds				

Table 2 - Anthropometric and lung function data for type 1 diabetic patients with mean duration of disease 6.92 \pm 1.8 (range 2-13) years compared with their matched controls.

Parameter	Diabetic patients (mean \pm SEM) (n=13)	Control subjects (mean \pm SEM) (n=13)	Percentage change (%)	p-value
Age (years)	33.46 \pm 3.81	30.92 \pm 3.62	-8.21	NS
Height (cm)	172.57 \pm 2.39	173.46 \pm 2.18	+0.15	NS
Weight (kg)	72.26 \pm 3.02	77.76 \pm 3.34	+7.07	NS
FVC (litres)	3.87 \pm 0.17	4.39 \pm 0.190	+11.84	NS
FEV ₁ (litres)	3.40 \pm 0.15	3.66 \pm 0.13	+7.10	NS
FEV ₁ /FVC%	88.10 \pm 1.96	83.53 \pm 1.10	-5.47	NS
FEF _{25-75%} (litres/s)	4.22 \pm 0.63	4.10 \pm 0.18	-2.92	NS
FEF _{75-85%} (litres/s)	1.61 \pm 0.20	1.36 \pm 0.13	-18.38	NS
PEF (litres/sec)	7.73 \pm 0.75	6.63 \pm 0.48	-16.59	NS
FVC - forced vital capacity, FEV ₁ - forced expiratory volume in one second, FEF - forced expiratory flow, PEF - peak expiratory flow, FEV ₁ /FVC% - forced expiratory ratio, NS - not significant, s - seconds				

Table 3 - Anthropometric and lung function data for type 1 diabetic patients with mean duration of disease 18.57 \pm 1.02 (range 15-30) years compared with their matched control.

Parameter	Diabetic patients (mean \pm SEM) (n=14)	Control subjects (mean \pm SEM) (n=14)	Percentage change (%)	p-value
Age (years)	46.57 \pm 4.04	47.21 \pm 4.77	+1.35	NS
Height (cm)	169 \pm 1.25	170.42 \pm 1.72	+0.83	NS
Weight (kg)	78.66 \pm 2.74	79.42 \pm 3.01	+0.95	NS
FVC (litres)	3.50 \pm 0.18	4.12 \pm 0.15	+15.04	p=0.02
FEV ₁ (litres)	2.81 \pm 0.19	3.38 \pm 0.15	+16.86	p=0.05
FEV ₁ /FVC%	80.29 \pm 3.40	81.92 \pm 1.41	+1.98	NS
FEF _{25-75%} (litres/s)	3.06 \pm 0.29	3.89 \pm 0.36	+21.33	NS
FEF _{75-85%} (litres/s)	1.22 \pm 0.15	1.12 \pm 0.15	-8.92	NS
PEF (litres/sec)	5.46 \pm 0.64	6.94 \pm 0.60	+21.32	NS
FVC - forced vital capacity, FEV ₁ - forced expiratory volume in one second, FEF - forced expiratory flow, PEF - peak expiratory flow, FEV ₁ /FVC% - forced expiratory ratio, NS - not significant, s - seconds				

Table 4 - Anthropometric and lung function data among type 1 diabetic patients with mean duration of disease 7.63 ± 1.14 (range 2-13) years compared with another group of matched type 1 diabetic patients with mean duration of disease 17.1 ± 0.62 (range 15-20) years.

Parameter	Diabetic patients with mean duration of disease 7.63 years (n=10)	Diabetic patients with mean duration of disease 17.1 years (n=10)	Percentage change (%)	P-value
Age (years)	36 ± 4.04	39.6 ± 3.64	-9.09	NS
Height (cm)	172.81 ± 2.71	168.7 ± 1.31	+2.43	NS
Weight (kg)	73.90 ± 3.34	77.23 ± 2.81	-4.31	NS
FVC (litres)	3.97 ± 0.18	3.71 ± 0.20	+7.00	NS
FEV ₁ (litres)	3.52 ± 0.16	2.92 ± 0.25	+20.55	$p=0.05$
FEV ₁ /FVC%	89.04 ± 1.51	77.85 ± 4.32	+14.37	$p=0.05$
FEF _{25-75%} (litres/s)	4.51 ± 0.35	3.13 ± 0.37	+44.08	$p=0.02$
FEF _{75-85%} (litres/s)	1.64 ± 0.22	1.24 ± 0.18	+32.25	NS
PEF (litres/sec)	8.40 ± 0.71	5.25 ± 0.79	+60.00	$p=0.01$

FVC - forced vital capacity, FEV₁ - forced expiratory volume in one second, FEF - forced expiratory flow, PEF - peak expiratory flow, FEV₁/FVC% - forced expiratory ratio, NS - not significant, s - seconds

that in the diabetic subjects, mean values for vital capacity, FEV₁, total lung capacity was similar to their predicted values. Their findings showed that type 1 diabetes mellitus does not affect pulmonary function. The most probable reason for the contradiction is that Maccioni and Colebatch studied the pulmonary function in 22 type 1 diabetic patients, but they did not consider the age, height, weight and sex matched control group, additionally, the number of diabetic patients was small. Therefore, our results contradict the results observed by Maccioni and Colebatch.

Schnapf et al.²⁹ conducted a study in type 1 diabetic patients with limited joint mobility and showed significantly decreased FVC and FEV₁, and also concluded that this decline in lung function could be due to decreased lung compliance or restriction of chest wall expansion. However, in our study we excluded subjects with limited joint mobility and observed a decreased FVC and FEV₁ in type 1 diabetic patients compared to their matched controls. Similarly, Cooper et al.³⁰ assessed the lung function in 35 nonsmoking adults with type 1 diabetes mellitus and reported that the total lung capacity in diabetic patients was lower than those recorded for the controls.

Davis et al.³¹ determined the association between diabetes mellitus and reduced lung function, and reported reduced FVC, FEV₁, VC, and PEF when expressed as a percentage of those predicted for age, sex, and height, the means of all spirometric measures, and a significant association of the duration of disease with FEV₁ and PEF.

We conclude that lung function in type 1 diabetic patients is impaired by a decrease in FVC and FEV₁ as compared to their matched controls. We also show that the longer the duration of disease, the

greater the lung function impairment. The findings are of importance in that they demonstrate the need for further prevention of lung damage. We advise therefore, that diabetic patients undergo periodic spirometry tests to assess the severity of lung function impairment. Spirometry will identify more susceptible diabetic patients so they can take additional preventive measures to further prevent the lung damage. These measures will help to prevent lung damage in initial stage, which often, over time, contribute to morbidity and mortality in diabetic patients. Additionally, physicians should contemplate the lung in the same way as other complications of diabetes mellitus, and recognize the size of the problem of pulmonary complications as a consequence of the novel techniques used through the respiratory tract in the treatment of diabetes mellitus such as insulin pump inhaler.

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